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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
BARTON, JEFFREY THOMAS	

ART UNIT	PAPER NUMBER
1753	

DATE MAILED: 04/20/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/928,590	SPENCE ET AL.	
	Examiner	Art Unit	
	Jeffrey T. Barton	1753	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *31 January 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *2-18,21-36,39-49 and 51-54* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *2-18,21-36 and 51-53* is/are rejected.

7)☒ Claim(s) *39-49 and 54* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *20050407, 20060224*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 31 January 2006 has been entered.

Response to Amendment

2. The amendment filed on 31 January 2006 does not place the application in condition for allowance.

Information Disclosure Statement

3. The Examiner thanks Applicant for providing the non-patent literature documents cited on the Information Disclosure Statement of 7 April 2005, which have now been considered.

Status of Rejections Pending Since the Office Action of 5 August 2005

4. All previous rejections are withdrawn due to Applicant's amendment.

Claim Objections

5. Claim 51 is objected to because in line 12 of the claim "a detection apparatus" is recited, although "a detection apparatus" was recited earlier at line 3. It is unclear whether this is intended to be the same detection apparatus. Appropriate correction is required.

Claim Rejections - 35 USC § 103

6. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

7. The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

8. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein

were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

9. Claims 51, 52, 2, 3, 5, 8-11, 13, 16-18, 21, 22, 25-29, and 31-36 are rejected under 35 U.S.C. 103(a) as being unpatentable over Blankenstein in view of Corio et al.

Regarding claim 51, Blankenstein discloses a microfluidic system (Figure 8; Page 2, lines 13-28) comprising (i) a substrate having an analysis unit microfabricated thereon (Page 19, lines 24-31), (ii) a detection apparatus (Figure 8, objective 16, photomultiplier tube), (iii) a processor (Figure 8, peak detector, Page 24, lines 31-36 - this procedure requires a processor such as that disclosed at Page 23 lines 17-28), and (iv) a flow control system (Syringe pumps 41, 42); wherein the analysis unit comprises a main channel (5) with an inlet, detection region downstream of the inlet (adjacent to microscope objective 16), and a branch point discrimination region (where channels 6 and 7 split) adjacent to and downstream of the detection region; two branch channels originating at the branch point in communication with the main channel (6 and 7); wherein the detection region comprises the detection apparatus as claimed (Figure 8; Page 24, lines 29-34); wherein the processor (Peak detector) is configured to receive a signal from the detection apparatus (Figure 8) and execute an algorithm based on the signal (Page 24, lines 29-34); and wherein the flow control system is responsive to the

processor (Page 24, lines 29-34) and is adapted to direct biological material into a selected branch channel (Page 24, lines 29-36), with the flow system having the capability of reversing the flow direction. (Page 24, line 36 - Page 25, line 4)

Regarding claim 52, Blankenstein discloses a flow control system responsive to a detection apparatus for evaluating the material according to a characteristic. (Page 24, lines 29-34)

Regarding claim 2, Blankenstein discloses a reservoir communicating with a branch channel. (Figure 8, chamber 37)

Regarding claim 3, Blankenstein discloses using a silicon substrate. (Page 19, lines 19-26)

Regarding claim 5, Blankenstein discloses the biological material comprising cells. (Page 18, lines 22-25)

Regarding claims 8 and 9, Blankenstein discloses electrophoretic and dielectrophoretic flow control. (Page 9, lines 15-20)

Regarding claim 10, Blankenstein discloses pressure-driven flow. (Figure 8, syringes cause flow)

Relevant to claim 11, Blankenstein discloses using valves in controlling fluid flow. (Figure 8, valves 43 and 44)

Regarding claim 13, Blankenstein discloses flow-stoppage-based control. (Page 24, lines 31-36)

Regarding claim 16, a pressure gradient inherently causes flow in the flow control method described at Page 24, lines 31-36.

Regarding claim 17, capillary action will inherently be present when flowing fluid between passages with differing cross section, as in the device shown in Figure 8. (e.g. Junction of channel 6 with chamber 37)

Regarding claim 18, Blankenstein discloses using valves for flow control. Figure 8, valves 43 and 44)

Regarding claims 21, 22, and 25, Blankenstein discloses optical detection of fluorescently labeled analytes. Such fluorescent labels are spectroscopically detectable. (Page 24, lines 8-18)

Regarding claim 26, Blankenstein discloses separation of cells according to size. (Page 19, lines 33-35)

Regarding claim 27, any surface on which the light impinges will cause scattering to some extent.

Regarding claims 28, 29 and 31, Blankenstein discloses using a light source and photomultiplier tube detector. (Page 24, lines 8-18)

Regarding claim 32, Blankenstein discloses such positioning of the detector. (Figure 8, objective 16 with associated PMT)

Regarding claims 33 and 34, Blankenstein discloses channel widths of 100-550 microns, with depths of 40-200 microns. (Page 20, line 33) Dimensions in the hundreds of microns correspond to the claimed dimensions, for separation of most mammalian cells.

Regarding claims 35 and 36, Blankenstein discloses separation due to fluorescent agents associated with the cells (Page 24, lines 8-9; Figure 7)

Blankenstein does not disclose the processor being configured to actuate the flow control system to reverse the flow of fluid in a branch channel. Specific to claim 11, Blankenstein also does not explicitly disclose using a "microvalve" for flow control.

Corio et al disclose a particle sorting apparatus in which all user interface functions are performed via a computer (i.e. processor) that controls all operations of the sorting apparatus. (Column 5, lines 50-64)

It would have been obvious to one having ordinary skill in the art at the time the invention was made to modify the system of Blankenstein by using a computer to control all detection and flow control operations (including the flow reversal disclosed by Blankenstein), as taught by Corio et al, because it would allow minimal operator assistance in performing tedious tasks, and provide added convenience through central control of all operation parameters. The desirability of such central control would have been quite obvious to anyone having ordinary skill in the art.

Despite changes to the claim wording, the limitations to flow reversal are still largely directed to the intended use of the apparatus. No structural difference can be seen between the system described by this combination and that of instant claim 51. A recitation of the intended use of the claimed invention must result in a structural difference between the claimed invention and the prior art in order to patentably distinguish the claimed invention from the prior art. If the prior art structure is capable of

performing the intended use, then it meets the claim. See *In re Casey*, 152 USPQ 235 (CCPA 1967) and *In re Otto*, 136 USPQ 458, 459 (CCPA 1963). Clearly, the device described by this combination would be capable of such function.

Regarding claim 11, particularly as there is no disclosure in the instant specification concerning any properties or requirements of such a "microvalve", this limitation is taken to be simply directed to the size of features of such a valve. One having ordinary skill in the art would certainly be motivated to use valves with channel dimensions on the order of the capillary dimensions (i.e. tens or hundreds of micrometers, like channels 5-7), in order to obtain precise flow control. Such valves could accurately be called "microvalves" based on this dimension. Furthermore, in *Gardner v. TEC Systems, Inc.*, 725 F.2d 1338, 220 USPQ 777 (Fed. Cir. 1984), *cert. denied*, 469 U.S. 830, 225 USPQ 232 (1984), the Federal Circuit held that, where the only difference between the prior art and the claims was a recitation of relative dimensions of the claimed device and a device having the claimed relative dimensions would not perform differently than the prior art device, the claimed device was not patentably distinct from the prior art device.

10. Claims 51, 52, 7, 8, 14, 15, and 28-30 are rejected under 35 U.S.C. 103(a) as being unpatentable over Ramsey et al in view of Corio et al.

Regarding claim 51, Ramsey et al disclose a microfluidic system (Figures 16 and 17) wherein said system comprises a substrate having an analysis unit microfabricated thereon, a detection apparatus, and a flow control system; wherein the analysis unit

comprises a main channel with an inlet, detection region downstream of the inlet (Column 7, lines 43-46), a branch point discrimination region adjacent to and downstream of the detection region (Figures 16 and 17), and two branch channels originating at the branch point in communication with the main channel (Figures 16 and 17); wherein the detection region comprises the detection apparatus as claimed (Column 7, lines 43-46); wherein the detection signal is used to execute a sorting algorithm based on the signal involving actuation of the flow control system (Column 7, lines 43-46); and wherein the flow control system is adapted to direct biological material into a selected branch channel (Column 7, lines 25-60), with the capability to reverse the flow direction. (Column 5, lines 2-5)

Regarding claim 52, Ramsey et al disclose a device where the flow control is responsive to a detector responsive to a characteristic of the analyte. (Column 7, lines 43-46, 56-60)

Regarding claims 7 and 8, Ramsey et al disclose electrophoretic and electroosmotic flow control. (Column 6, lines 36-50)

Regarding claims 14 and 15, Ramsey et al disclose flow control by a voltage gradient between the branch channels and junction, caused by electrodes in the branch channels. (Column 3, lines 62-64; Column 8, lines 50-53)

Regarding claim 20, Ramsey et al disclose reversible flow. (Column 5, lines 2-5)

Regarding claims 28-30, Ramsey et al disclose a detection apparatus comprising source and detector (CCD) for electromagnetic radiation. (Column 3, line 65 - Column 4, line 4)

Ramsey et al do not disclose a processor that is configured to receive the detection signal and execute the algorithm, or actuate the flow control system to reverse the flow of fluid in a branch channel.

Corio et al disclose a particle sorting apparatus in which all user interface functions are performed via a computer (i.e. processor) that controls all operations of the sorting apparatus, including the sorting algorithm, based on the detected presence or absence of a particle of interest. (Column 5, lines 50-64)

It would have been obvious to one having ordinary skill in the art at the time the invention was made to modify the system of Ramsey et al by using a computer to control all detection and flow control operations, as taught by Corio et al, because it would allow minimal operator assistance in performing tedious tasks, and provide added convenience through central control of all operation parameters. The desirability of such central control would have been quite obvious to anyone having ordinary skill in the art.

In such a combination, applied voltages to the various channels would be controlled through the computer, and reversal of the voltages as disclosed by Ramsey would result in the claimed flow reversal. Any computer-controlled voltage source would be capable of such operation, and thus the processor would be "configured" as claimed.

Despite changes to the claim wording, the limitations to flow reversal are still largely directed to the intended use of the apparatus. No structural difference can be seen between the system described by this combination and that of instant claim 51. A recitation of the intended use of the claimed invention must result in a structural difference between the claimed invention and the prior art in order to patentably distinguish the claimed invention from the prior art. If the prior art structure is capable of performing the intended use, then it meets the claim. See *In re Casey*, 152 USPQ 235 (CCPA 1967) and *In re Otto*, 136 USPQ 458, 459 (CCPA 1963). Clearly, the device described by this combination would be capable of such function.

11. Claim 3 is rejected under 35 U.S.C. 103(a) as being unpatentable over Ramsey et al and Corio et al as applied to claim 51 above, and further in view of Parce et al. (US 5,779,868)

Ramsey et al and Corio et al disclose a device as described above in addressing claim 51.

Neither Ramsey et al nor Corio et al explicitly disclose constructing the channels in a silicon substrate.

Parce et al disclose fabrication of capillary channels for analytical devices in a silicon substrate using well-known lithographic techniques. (Column 4, lines 6-56)

It would have been obvious to one having ordinary skill in the art at the time the invention was made to further modify the device of Ramsey et al by fabricating the

substrate from silicon, as taught by Parce et al, because the lithographic techniques were well-known, reliable, and suitable for large-scale production.

12. Claims 4, 6, and 53 are rejected under 35 U.S.C. 103(a) as being unpatentable over Ramsey et al and Corio et al as applied to claim 51 above, and further in view of Parce et al. (US 5,885,470)

Ramsey et al and Corio et al disclose a device as described above in addressing claim 51.

Neither Ramsey et al nor Corio et al explicitly disclose constructing the channels from silicone elastomers (Claim 4) or specifically polydimethylsiloxane (PDMS) (Claim 53); or molding the substrates by impression from an etched silicon mold. (Claim 6)

Parce et al disclose molding substrates with capillary channels for analytical devices from silicone elastomers (specifically PDMS) (Column 5, lines 16-67), and molding the devices by impression from an etched silicon wafer mold. (Column 13, lines 44-57)

It would have been obvious to one having ordinary skill in the art at the time the invention was made to further modify the device of Ramsey et al by replacing his glass substrate for a PDMS substrate molded against an etched silicon mold, as taught by Parce et al, because it would allow low-cost, large scale fabrication of the devices.

13. Claim 12 is rejected under 35 U.S.C. 103(a) as being unpatentable over Blankenstein and Corio et al as applied to claim 51 above, and further in view of Gourley et al.

Blankenstein and Corio et al disclose a device as described above in addressing claim 51. Blankenstein also discloses using various forces to sort cells, including magnetic, gravitational, and hydrodynamic forces.

Neither Blankenstein nor Corio et al explicitly disclose separation of cells using optical trapping.

Gourley et al disclose a similar cell sorting device wherein cells of different types are directed towards their desired destination using optical trapping. (Column 7, line 50 - Column 8, line 7)

It would have been obvious to one having ordinary skill in the art at the time the invention was made to further modify the device of Blankenstein by incorporating a device to aid in sorting cells using optical trapping, as taught by Gourley et al, because Gourley teaches the effectiveness of using optical trapping for cell sorting, and one having ordinary skill in the art would have recognized that superior precision would be attainable with optical trapping, as direct manipulation of a cell is used in sorting, as opposed to control of the flow of a fluid in which the cell is suspended.

14. Claims 22-24, 35, and 36 are rejected under 35 U.S.C. 103(a) as being unpatentable over Ramsey et al and Corio et al as applied to claims 51 and 52 above, and further in view of Asgari et al.

Ramsey et al and Corio et al disclose a device as described above in addressing claims 51 and 52.

Relevant to claims 22 and 35, Ramsey et al also disclose detection of fluorescence from analytes. (Column 4, lines 1-9)

Relevant to claim 36, Ramsey et al disclose electroosmotic and electrophoretic flow control. (Column 6, lines 35-50)

Neither Ramsey et al nor Corio et al explicitly disclose detection and selection of cells based on fluorescent, chemiluminescent, or radioactive reporters (Claims 22-24), nor do they disclose labeling cells for analysis with a fluorescent label (or any label). (Claim 35)

Asgari et al disclose labeling, detection, and selection of cells labeled with fluorescent, chemiluminescent or radioactive reporters. (Column 3, lines 18-21; Column 21, line 54 - Column 22, line 35)

It would have been obvious to one having ordinary skill in the art at the time the invention was made to further modify the device of Ramsey et al by labeling cells to be analyzed with characteristic reporters (and providing suitable detectors), as taught by Asgari et al, because such detection methods are conventional, and it would allow the device to be used to analyze a wider variety of cells, and separate them based on a wider variety of characteristics. In addition, fluorescent labels would provide especially convenient interrogation means, given the disclosed detector of Ramsey et al.

Allowable Subject Matter

15. Claims 54 and 39-49 are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

16. The following is an examiner's statement of reasons for allowance:

Claim 54 has been amended to recite steps of "directing at least one cell out of the selected branch channel so that it passes through the detection region a second time" and "interrogating the cell a second time". None of the prior art.of record teaches or suggests such a method. Although Blankenstein teaches sorting though multiple branch points (e.g. Embodiments of Figure 9), these use multiple detection points for discrimination. There is no suggestion or motivation for directing cells to the same detection point more than one time. Therefore, the claims are considered to distinguish over the prior art of record.

Any comments considered necessary by applicant must be submitted no later than the payment of the issue fee and, to avoid processing delays, should preferably accompany the issue fee. Such submissions should be clearly labeled "Comments on Statement of Reasons for Allowance."

Response to Arguments

17. Applicant's arguments submitted 31 January 2006 have been considered but are moot in view of the new ground(s) of rejection.

Conclusion

18. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Dr. Jeffrey Barton, whose telephone number is (571) 272-1307. The examiner can normally be reached Monday-Friday from 9:00 am – 5:30 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Nam Nguyen, can be reached at (571) 272-1342. The fax number for the organization where this application or proceeding is assigned is (571) 273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at (866) 217-9197 (toll-free).

JTB
14 April 2006

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